Report Documentation Page

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1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
20 FEB 2014	**Final**	**27 Feb 2013 - 20 Feb 2014**

4. TITLE AND SUBTITLE
FDG20130020A "Pilot study of the efficacy of extracellular matrix arterial interposition grafts in a sheep (Ovis aries) model."

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER
FDG20130020A

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535

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9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535

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11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

bjective: The purpose of this study was to compare early patency and histology of Cormatrix small intestine submucosa interposition grafts in carotid arteries in sheep. Methods: Three crossbred sheep were anesthetized, instrumented, and had 10 cm interposition grafts placed in both carotid arteries via a midline neck incision. The grafts were created with CorMatrix extracellular matrix. The wounds were closed and the animals recovered. Lovenox was administered starting post-operatively daily for the remainder of the experiment. Duplex ultrasonography was conducted at 1 and 6 weeks, followed by thorough necropsy and histologic evaluation of the grafts using hematoxylin and eosin and Massons Trichrome stains. Results: Following surgery, two animals had uncomplicated courses without clinical evidence of thrombosis or wound complication. The third animal succumbed from graft failure secondary to a postoperative seroma and wound infection. Duplex examinations revealed patent fistulas with normal vessel diameters, flow velocities, and spectral patterns. Upon post mortem, there was a lack of perivascular inflammation and tissue reaction. Histologic assessment confirmed patency without evidence of thrombosis or inflammatory infiltration. The ECM was well populated with cells and near complete luminal endothelial cell coverage was present by four weeks. Conclusion: In this pilot study, the Cormatrix extracellular matrix performed well in a sheep carotid interposition graft model.

15. SUBJECT TERMS
US Air Force, Medical Service, Medical Research, Graduate Medical Education

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
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60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20130020A **DATE:** 18 February 2014

PROTOCOL TITLE: Pilot study of the efficacy of extracellular matrix arterial interposition grafts in a sheep (*Ovis aries*) model

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Lt Col Daren Danielson

DEPARTMENT: Cardiothoracic Surgery **PHONE #:** 423-5179

INITIAL APPROVAL DATE: 27 February 2013 **LAST TRIENNIAL REVISION DATE:**

FUNDING SOURCE: SGO

1. **RECORD OF ANIMAL USAGE:**

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Ovis aries	3	3	3

2. **PROTOCOL TYPE / CHARACTERISTICS:** (Check all applicable terms in **EACH** column)

___ Training: Live Animal	___ Medical Readiness	___ Prolonged Restraint
___ Training: non-Live Animal	___ Health Promotion	___ Multiple Survival Surgery
_X_ Research: Survival (chronic)	___ Prevention	___ Behavioral Study
___ Research: non-Survival (acute)	___ Utilization Mgt.	___ Adjuvant Use
___ Other ( )	_X_ Other (Treatment)	___ Biohazard

3. **PROTOCOL PAIN CATEGORY (USDA):** (Check applicable) ___ C _X_ D ___ E

4. **PROTOCOL STATUS:**

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

_X_ Completed, all approved procedures/animal uses have been completed

5. **FUNDING STATUS:** Funding allocated: $10,080.00 Funds remaining: $ 0.00

6. **PROTOCOL PERSONNEL CHANGES:**

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? ___ Yes _X_ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

_____

_____

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

_____

_____

7. **PROBLEMS / ADVERSE EVENTS:** Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

Of the 3 sheep used in the protocol, one developed a postoperative seroma that became infected despite aggressive treatment. The graft site dehisced and the sheep experience a fatal event.

8. **REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:**

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

No. The sheep remains the best model for this study due to the length of their carotid arteries.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

No.

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No. A pilot study was used to minimize the number of animals used.

9. **PUBLICATIONS / PRESENTATIONS:** (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

None

10. **Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?**

Yes. This pilot protocol demonstrated that bilateral carotid interposition grafts could be safely performed in sheep and that the proposed model using porcine small intestinal submucosa extracellular matrix can be used for these repairs.

11. **PROTOCOL OUTCOME SUMMARY:** (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objective: The purpose of this study was to compare early patency and histology of Cormatrix™ small intestine submucosa interposition grafts in carotid arteries in sheep.
Methods: Three crossbred sheep were anesthetized, instrumented, and had 10 cm interposition grafts placed in both carotid arteries via a midline neck incision. The grafts were created with CorMatrix™ extracellular matrix. The wounds were closed and the animals recovered. Lovenox was administered starting post-operatively daily for the remainder of the experiment. Duplex ultrasonography was conducted at 1 and 6 weeks, followed by thorough necropsy and histologic evaluation of the grafts using hematoxylin and eosin and Masson's Trichrome stains.
Results: Following surgery, two animals had uncomplicated courses without clinical evidence of thrombosis or wound complication. The third animal succumbed from graft failure secondary to a postoperative seroma and wound infection. Duplex examinations revealed patent fistulas with normal vessel diameters, flow velocities, and spectral patterns. Upon post mortem, there was a lack of perivascular inflammation and tissue reaction. Histologic assessment confirmed patency without evidence of thrombosis or inflammatory infiltration. The ECM was well populated with cells and near complete luminal endothelial cell coverage was present by four weeks.
Conclusion: In this pilot study, the Cormatrix extracellular matrix performed well in a sheep carotid interposition graft model.